

wherein:

each B is a nucleobase;

one of X<sub>1</sub> or X<sub>2</sub> is O, and the other of X<sub>1</sub> or X<sub>2</sub> is S;

each R<sub>1</sub>, is, independently, H, hydroxyl, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>3</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, halogen, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

or R<sub>1</sub> is a group of formula Z-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

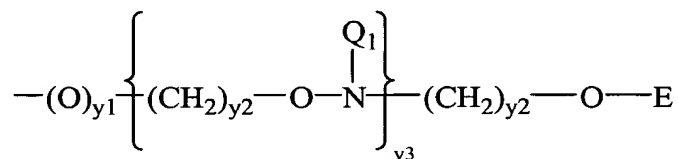
Z is O, S, NH, or N-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

R<sub>22</sub> is C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, or C<sub>2</sub>-C<sub>20</sub> alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

v is from 0 to about 10;

or R<sub>1</sub> has the formula:



wherein:

y<sub>1</sub> is 0 or 1;

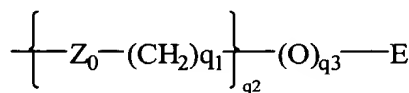
y<sub>2</sub> is independently 0 to 10;

y<sub>3</sub> is 1 to 10;

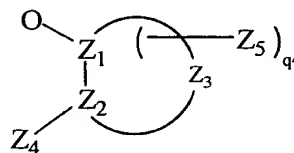
E is C<sub>1</sub>-C<sub>10</sub> alkyl, N(Q<sub>1</sub>)(Q<sub>2</sub>) or N=C(Q<sub>1</sub>)(Q<sub>2</sub>);

each Q<sub>1</sub> and Q<sub>2</sub> is, independently, H, C<sub>1</sub>-C<sub>10</sub> alkyl, substituted alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support; or Q<sub>1</sub> and Q<sub>2</sub>, together, are joined in a nitrogen protecting group or a ring structure that can include at least one additional heteroatom selected from N and O;

or R<sub>1</sub> has one of formula I or II:



I



II

wherein:

$Z_0$  is O, S, or NH;

$q^1$  is from 0 to 10;

$q^2$  is from 1 to 10;

$q^3$  is 0 or 1;

$q^4$  is, 0, 1 or 2;

$Z_4$  is  $OM_1$ ,  $SM_1$ , or  $N(M_1)_2$ ;

each  $M_1$  is, independently, H,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  haloalkyl,  $C(=NH)N(H)M_2$ ,  $C(=O)N(H)M_2$  or  $OC(=O)N(H)M_2$ ;

$M_2$  is H or  $C_1$ - $C_8$  alkyl;

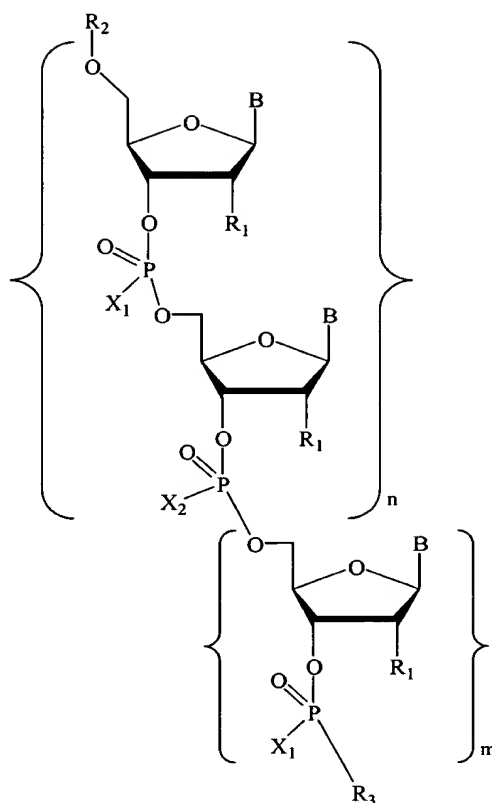
$Z_1$ ,  $Z_2$  and  $Z_3$  comprise a ring system having from about 4 to about 7 carbon atoms, or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur, and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic; and

$Z_5$  is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms,  $N(Q_1)(Q_2)$ ,  $OQ_1$ , halo,  $SQ_1$  or CN;

$n$  is from 2 to 50; and

$m$  is 0 or 1.

29. (amended twice) A method of treating an organism having a disease characterized by the undesired production of a protein, said method comprising contacting said organism with a compound of formula:



wherein:

each B is a nucleobase;

$X_1$  is S;

$X_2$  is O;

each  $R_1$ , is, independently, H, hydroxyl,  $C_1$ - $C_{20}$  alkyl,  $C_3$ - $C_{20}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl, halogen, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

or  $R_1$  is a group of formula  $Z-R_{22}-(R_{23})_v$ ;

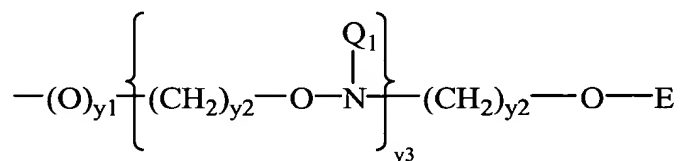
Z is O, S, NH, or N- $R_{22}-(R_{23})_v$ ;

R<sub>22</sub> is C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, or C<sub>2</sub>-C<sub>20</sub> alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

v is from 0 to about 10;

or R<sub>1</sub> has the formula:



y<sub>1</sub> is 0 or 1;

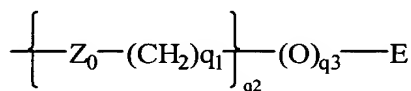
y<sub>2</sub> is independently 0 to 10;

y<sub>3</sub> is 1 to 10;

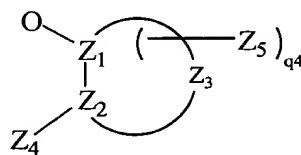
E is C<sub>1</sub>-C<sub>10</sub> alkyl, N(Q<sub>1</sub>)(Q<sub>2</sub>) or N=C(Q<sub>1</sub>)(Q<sub>2</sub>);

each Q<sub>1</sub> and Q<sub>2</sub> is, independently, H, C<sub>1</sub>-C<sub>10</sub> alkyl, substituted alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support; or Q<sub>1</sub> and Q<sub>2</sub>, together, are joined in a nitrogen protecting group or a ring structure that can include at least one additional heteroatom selected from N and O;

or R<sub>1</sub> has one of formula I or II:



I



II

wherein:

Z<sub>0</sub> is O, S, or NH;

$q^1$  is from 0 to 10;

$q^2$  is from 1 to 10;

$q^3$  is 0 or 1;

$q^4$  is, 0, 1 or 2;

$Z_4$  is  $OM_1$ ,  $SM_1$ , or  $N(M_1)_2$ ;

each  $M_1$  is, independently, H,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  haloalkyl,  $C(=NH)N(H)M_2$ ,  $C(=O)N(H)M_2$  or  $OC(=O)N(H)M_2$ ;

$M_2$  is H or  $C_1$ - $C_8$  alkyl;

$Z_1$ ,  $Z_2$  and  $Z_3$  comprise a ring system having from about 4 to about 7 carbon atoms, or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur, and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic; and

$Z_5$  is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms,  $N(Q_1)(Q_2)$ ,  $OQ_1$ , halo,  $SQ_1$  or  $CN$ ;

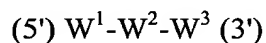
$n$  is from 2 to 50; and

$m$  is 0 or 1;

$R_2$  is H, a hydroxyl protecting group, or an oligonucleotide; and

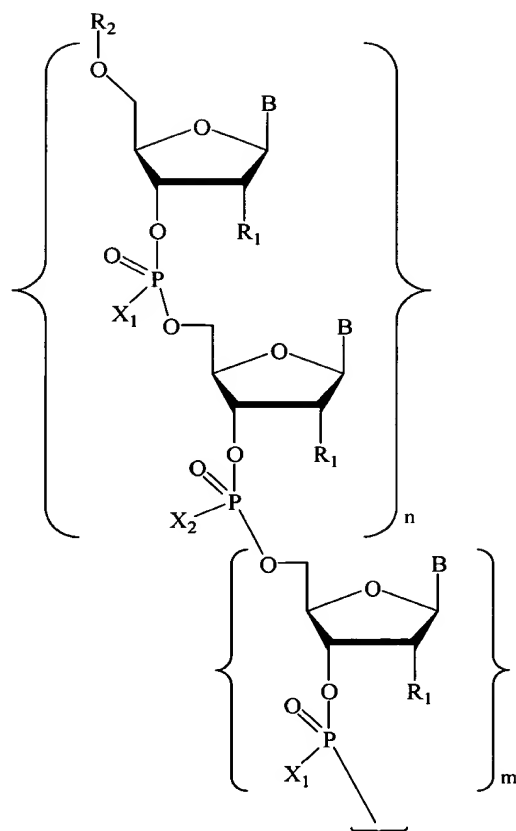
$R_3$  is OH, an oligonucleotide, or a linker connected to a solid support.

30. (amended twice) A method of treating an organism having a disease characterized by the undesired production of a protein, said method comprising contacting said organism with a compound of formula:



wherein:

$W^1$  has the Formula:



wherein:

each B is a nucleobase;

one of X<sub>1</sub> or X<sub>2</sub> is O, and the other of X<sub>1</sub> or X<sub>2</sub> is S;

each R<sub>1</sub>, is, independently, H, hydroxyl, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>3</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, halogen, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

or R<sub>1</sub> is a group of formula Z-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

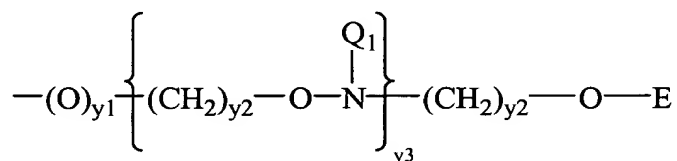
Z is O, S, NH, or N-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

R<sub>22</sub> is C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, or C<sub>2</sub>-C<sub>20</sub> alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

v is from 0 to about 10;

or R<sub>1</sub> has the formula:



y<sub>1</sub> is 0 or 1;

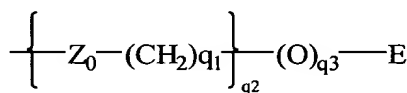
y<sub>2</sub> is independently 0 to 10;

y<sub>3</sub> is 1 to 10;

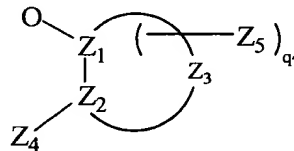
E is C<sub>1</sub>-C<sub>10</sub> alkyl, N(Q<sub>1</sub>)(Q<sub>2</sub>) or N=C(Q<sub>1</sub>)(Q<sub>2</sub>);

each Q<sub>1</sub> and Q<sub>2</sub> is, independently, H, C<sub>1</sub>-C<sub>10</sub> alkyl, substituted alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support; or Q<sub>1</sub> and Q<sub>2</sub>, together, are joined in a nitrogen protecting group or a ring structure that can include at least one additional heteroatom selected from N and O;

or R<sub>1</sub> has one of formula I or II:



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wherein:

Z<sub>0</sub> is O, S, or NH;



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$Z_4$  is  $OM_1$ ,  $SM_1$ , or  $N(M_1)_2$ ;

each  $M_1$  is, independently, H,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  haloalkyl,  $C(=NH)N(H)M_2$ ,  $C(=O)N(H)M_2$  or  $OC(=O)N(H)M_2$ ;

$M_2$  is H or  $C_1$ - $C_8$  alkyl;

$Z_1$ ,  $Z_2$  and  $Z_3$  comprise a ring system having from about 4 to about 7 carbon atoms, or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur, and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic; and

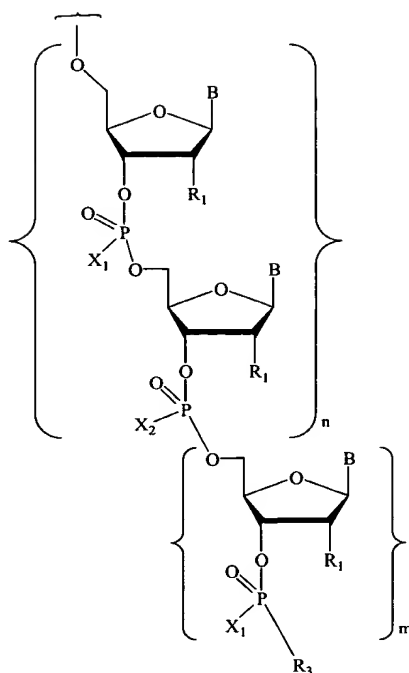
$Z_5$  is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms,  $N(Q_1)(Q_2)$ ,  $OQ_1$ , halo,  $SQ_1$  or CN;

$n$  is from 2 to 50; and

$m$  is 0 or 1;

$R_2$  is H, a hydroxyl protecting group, or an oligonucleotide;

$W^3$  has the Formula:



wherein  $R_3$  is OH, an oligonucleotide, or a linker connected to a solid support; and

$W^2$  is a plurality of covalently bound nucleosides linked by phosphodiester or phosphorothioate linkages.

### REMARKS

Claims 28-30 and 34-51 are pending in this application.

Claims 28-30 have been amended, support for which can be found throughout the specification and in the original claims. No new matter has been added.

As a preliminary matter, Applicant wishes to thank the Examiner for pointing out that his issued U.S. Patent No. 6,326,358, of which the present application is a division, contains a printer's error; the middle structure illustrated in claim 1 should contain the moiety " $X_2$ " and not " $X_1$ " as printed. Applicant has, or will be shortly, submitting a certificate of correction to rectify this error.